(A) using atomic coordinates obtained from crystallographical analysis of a catalytic domain of a TACE polypeptide to design an associating compound that forms a bond with said catalytic domain;

(B) synthesizing said compound; and

(C) determining *in vitro* whether said compound associates with said catalytic domain.

Please amend the following claims:

43. (Twice Amended) The method according to claim 63, wherein the atomic coordinates comprise the coordinates of Table 1, or a substantial part thereof.

51. (Twice Amended) The method according to claim 63, wherein said crystallographical analysis employs a TACE polypeptide crystal that diffracts to 2.0 Å.

52. (Twice Amended) The method according to claim 63, wherein said crystallographical analysis employs a TACE polypeptide crystal that is monoclinic.

53. (Twice Amended) The method according to claim 63, wherein said crystallographical analysis employs a TACE polypeptide crystal having a unit cell comprising four crystallographically independent TACE catalytic domain (TCD) molecules.

55. (Twice Amended) The method according to claim 63, wherein said crystallographical analysis employs a TACE polypeptide crystal belonging to the monoclinic space group $P2_1$ and having cell constants a=61.38 Å, b=126.27 Å, c=81.27 Å, and β=107.41°.

63. (Amended) A method of identifying a compound that associates with tumor necrosis factor-α-converting enzyme (TACE), comprising:

(A) using atomic coordinates obtained from crystallographical analysis of a catalytic domain of a TACE polypeptide to design an associating compound that forms a bond with said catalytic domain; and

(B) determining via computer-generated models whether said compound associates with said catalytic domain.

64. (Amended) A method of identifying a compound that associates with tumor necrosis factor-α-converting enzyme (TACE), comprising:

(A) using atomic coordinates obtained from crystallographical analysis of a catalytic domain of a TACE polypeptide to design an associating compound that forms a bond with said catalytic domain; and

(B) determining via computer-generated models whether said compound associates with said catalytic domain,

wherein said atomic coordinates comprise the coordinates of Table 1, or a substantial part thereof, and said associating compound is a TACE inhibitor.

65. (Amended) A method of identifying a compound that associates with tumor necrosis factor-α-converting enzyme (TACE), comprising:

(A) using atomic coordinates obtained from crystallographical analysis of a catalytic domain of a TACE polypeptide to design an associating compound that forms a bond with said catalytic domain; and

(B) determining via computer-generated models whether said compound associates with said catalytic domain,

wherein said atomic coordinates comprise the coordinates of Table 1, or a substantial part thereof, and said associating compound is designed to introduce a non-polar group which occupies the S1' pocket of TNF-α-converting enzyme.

B5

REMARKS

Applicants thank Examiner Zeman for the courtesy of an interview held in her office on October 15, 2001.

Claims 1-39, which were previously withdrawn following a restriction requirement, are hereby cancelled. Claim 44 also has been cancelled, and claims 43, 51-53, 55 and 63-65 have been amended. Accordingly, Claims 41-43, 45-66 are pending.

In compliance with 37 C.F.R. § 1.121(b-c), Applicants enclose marked up versions of the amended claims and specification, showing all of the relative changes.

I. OBJECTIONS

The Examiner requests that Applicants update the priority information at the beginning of the specification. Applicants have complied with the request and assert that the objection has been obviated.

The Examiner objects to the specification for failing to label, by unique sequence identifier, sequences with four or more amino acids. Applicants concurrently submit replacement sections of